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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/716,924	11/19/2003	Colin Louis Masters	9287ZYA	6426

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EXAMINER	
CHERNYSHEV, OLGA N	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 06/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/716,924	MASTERS ET AL.	
	Examiner	Art Unit	
	Olga N. Chernyshev	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 November 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/15/3*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of CP94 as species in the reply filed on May 16, 2005 is acknowledged. The traversal is on the ground(s) that all recited species possess the same property as being able to cross the blood brain barrier and modulate the interaction as recited in the pending claims and that "CP94 is simply an example of such agents". Applicant is reminded that in cases when traversal of the restriction requirement is limited to the grounds that the species are not patentably distinct, Applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

The requirement is still deemed proper and is therefore made FINAL.

Claims 25-42 are under examination in the instant office action.

Drawings

2. Figures 7 and 9 of the instant application are presented on separate pages or in separate panels. 37 C.F.R. § 1.84(u) (1) states that in cases when figures present partial views of a drawing, which are intended to form one complete view, whether contained on one or several sheets, the figures must be identified by the same number followed by a capital letter. Applicant is reminded that once the drawings are changed to meet the separate numbering requirement of 37 C.F.R. § 1.84(u) (1), the specification should be amended to change the Brief Description of the Drawings and the rest of the specification

to refer to each Figure accordingly. If, for example, Figure 7 is divided into Figures 7A-7B, then the Brief Description and all the references to this figure in the specification must refer to this Figure in the same manner.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 25-42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 25-42 are directed to methods of treating Alzheimer's disease in a patient by administration of an agent that modulates the interaction within the central nervous system between a divalent or trivalent cation and/or heparin with amyloid precursor protein (APP). First, Applicant is advised that claims 25-26, 31-32 and 37-38 are single means claims in that they recite "an agent [which] modulates the interaction within the central nervous system between a divalent or trivalent cation and/or heparin with amyloid precursor protein", which, by broadest reasonably interpretation encompasses any known factor, including lethal drugs. MPEP 2164.08(a) defines a single means claim as a claim which covered every conceivable means for achieving the stated purpose when the specification disclosed at most only those means known to the inventor. This type of

claim was held to be nonenabling for the scope of the claim in *In re Hyatt* , 708 F.2d 712, 218 USPQ 195 (Fed. Cir. 1983) because the specification disclosed at most only those means known to the inventor. When claims depend on a recited property, a fact situation comparable to *Hyatt* is possible, where the claim covers every conceivable structure (means) for achieving the stated property (result) while the specification discloses at most only those known to the inventor. This appears to be the instant case and the claims are not commensurate in scope with the specification.

Next, with respect to claims 27-30, 33-36 and 39-42, which are limited to using a zinc-binding agents to treat Alzheimer's disease, the instant specification fails to provide enough guidance for one skilled in the art on how to practice the instant methods, thereby requiring undue experimentation to discover how to use Applicant's invention, as currently claimed.

The factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. *In re Wands*, 8 USPQ2d, 1400 (CAFC 1988).

The nature of the invention is the demonstration that zinc and heparin are capable to bind to a specific portion of APP (figure 7 and pages 21-22 of the instant specification), that zinc abolishes the binding of heparin to APP, which is asserted to be a beneficial effect of heparin (pages 31-32) and that addition of zinc to the diet of two

Alzheimer's patients significantly worsen their condition (Examples 3 and 6 on pages 26-27 and 32-33 of the specification) as compared to two healthy elderly volunteers.

At the time of invention, it was not recognized in the art that zinc plays a critical role in the etiology of Alzheimer's disease. Alzheimer's disease (AD) is known to be characterized by behavioral changes related to memory loss and impairment of cognition and by two types of morphological brain abnormalities, such as the presence of neurofibrillary tangles (NFT) in neurons of the cortex and extracellular deposits of amyloid-β protein, Aβ (see Goedert et al., 1991, Current Opinion in Neurobiology, 1, pp. 441-447 for review, for example). With respect to zinc metabolism, the role of zinc with association to Alzheimer's disease was not well understood (see middle at page 33 of the instant specification); however, article of Constantinidis (Constantinidis, Drug Development Research, 1992, 27, pp. 1-14) describes the positive results of treatment of AD patients with zinc supplements, which showed clear improvement of memory, understanding and communication (see pages 8-9). The author makes a conclusion that zinc has a beneficial effect for AD patients and that zinc deficiency may result in acceleration of abnormal production of NFT (see page 2 and the whole paper).

Thus, the state of the art can be characterized as (1) recognizing that NFT and Aβ plaques constitute two major brain abnormalities in AD pathology and (2) recognizing controversy of the existing reports regarding studies on role of zinc in AD.

While the skill level in the art is high, the level of predictability is low. Enzymatic processing of amyloid precursor protein (APP), which, under pathological conditions results in production of Aβ, is a complex process not limited to effects of zinc or heparin binding. The sole working examples in the specification, as originally filed, pertain to the

in vitro binding experiments. Furthermore, while it is not necessary that Applicant understands or discloses the mechanism by which the invention functions, in this case, in the absence of such an understanding, no extrapolation can be made of the results of limited *in vitro* protein binding studies to the claimed method of treatment of Alzheimer's disease. Moreover, one skilled in the art readily appreciates that no factual evidence or sound scientific reasoning has been provided in the instant specification to support a conclusion that administration of zinc-binding agents could be effective to treat Alzheimer's disease solely based on the finding that excess of zinc caused significant worsening of symptoms of two AD patients.

Applicant's invention is predicated on the finding that zinc and heparin are capable to bind APP, a precursor molecule of Aβ, and that increased zinc in the diet of two Alzheimer's patients significantly worsen their condition. Applicant further extrapolates these results into a method for treatment of Alzheimer's disease by administration of zinc-binding agents. Accordingly, it would appear that Applicant provides a single finding (the finding), and then presents an invitation to assay if zinc binding affects amyloid plaque formation, then to experiment to determine if administration of zinc-binding agents would have any effect on the progression of Alzheimer's disease in general or on what particular symptoms, and then to establish regimes of treatment, such as routes, duration and therapeutically effective amounts suitable for the claimed treatment. A skilled practitioner would clearly have to engage in a sufficient amount of undue experimentation in order to be able to practice the instant invention, especially in view of art recognition that zinc deficiency increases burden of

NFT, the second major morphological abnormality of AD, and, therefore, would reasonably expected to aggravate the progression of AD.

A patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. In the decision of *Genentec, Inc, v. Novo Nordisk*, 42 USPQ 2d 100,(CAFC 1997), the court held that: "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" and that "[t]ossing out the mere germ of an idea does not constitute enabling disclosure". The court further stated that "when there is no disclosure of any specific starting material or of any of the conditions under which a process is to be carried out, undue experimentation is required; there is a failure to meet the enablement requirements that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art", "[i]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".

The instant specification is not enabling because one can not following the guidance presented therein and practice the claimed method without first making a substantial inventive contribution.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 28-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. Claims 28 and 40 recite the limitation "zinc-binding agent" in claims 25 and 37, respectively. There is insufficient antecedent basis for this limitation in the claims.

6. Claim 31 is vague and indefinite for recitation "altering [...] digestion". The term "altering" is a relative term, which requires a point of reference as to what is considered non-altered state of digestion.

7. Claims 31 and 37 are vague and ambiguous for recitation "an effective amount" without stating an objective as what the amount is effective for.

8. Also, recitation "administration to said patient to an effective amount" in claims 31 and 37 appears to be lacking sense. Clarification is required.

9. Claim 37 is vague and indefinite for recitation "incorrect [...] processing". The metes and bounds of the limitation cannot be determined from the claim or the instant specification, especially in view of the absence of information on what constitutes the "correct" processing of APP.

10. Claims 29-30, 32-36, 38-39 and 41-42 are indefinite for being dependent from indefinite claims.

Claim Rejections - 35 USC § 102

11. With respect to claims 29, 35 and 41, which recite sodium citrate as a zinc-binding agent, Applicant is advised that these claims encompass consumption of commonly known popular beverages, such as ice-tea and soda, which all contain certain amounts of sodium citrate.

Conclusion

12. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (571) 272-0870. The examiner can normally be reached on 8:00 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony C. Caputa can be reached on (571) 272-0829. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 872-9306. If this number is out of service, please call the Group receptionist for an alternative number. Faxed draft or informal communications with the examiner should be directed to (571) 273-0870. Official papers should NOT be faxed to (571) 273-0870.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Olga N. Chernyshev, Ph.D.
Primary Examiner
Art Unit 1646

June 7, 2005